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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,968	03/19/2007	Michael Josephus Van Eijk	VAN EIJK17	2423

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,968	VAN EIJK, MICHAEL JOSEPHUS	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 3/13/09 to the Office action has been entered. Claims 32-72 are pending.

Election/Restrictions

1. The applicants' traverse filed 3/13/09 is persuasive. Claims 32-72 are examined together.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 39-48 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 39-43 are vague and indefinite because it is unclear whether the GC content is the total GC content from C1 and C2. Clarification is required.

b. Claims 44-48 are vague and indefinite because of the phrase "comparable length". It is unclear what is meant the phrase.

c. Claim 53 is vague and indefinite because of the phrase "stuffer sequence". It is unclear what is meant by the phrase.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 32-33, 35-41, 44-52, 54-56 and 58-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Hogan et al. (5424413, issued, Jun. 13, 1995).

Hogan et al. disclose a nucleic acid hybridization probe and method of use. The probe comprises two separate target-specific regions that hybridize to a target nucleic acid sequence and at least two distinct arm regions that do not hybridize with the target nucleic acid but possess complementary regions that are capable of hybridizing with one another (see column 1, lines 51-58 and fig. 2A) to form a duplex in the presence of target nucleic acid (see column 1, lines 58-66 and column 2, lines 59-62). The duplex has a Tm at least 4^0C (or 7^0C or even 10^0C) which is greater than the hybridization temperature to a target nucleic acid (see column 2, lines 60-63). The GC content of both arms ranges from 50%-100% (see fig. 2A). The GC content of some arms is more than 60% (see fig. 3A, 132 strand) and 70% (see fig. 3B, 135 strand). C1 or C2 comprises at least one C nucleotide more than C nucleotides in T1 or T2 (see fig 2A, strand 2) or at least two, three or four G nucleotides more than G nucleotides in T1 or T2 (see fig. 2A, strand 1) or at least five G nucleotides more than G nucleotides in T1 or T2 (see fig. 18, strand 1). The strand of the probe has chemically modified bases (see column 2, lines and column 6, lines 10-19). The length of the arm is 8 to 20 contiguous complementary bases (see column 8, lines 9-11). The arm region is designed to have a site for extension by a polymerase (see column 21, lines 46-48 and column 38, lines 40-44). The regions which are complementary to a target nucleic acid include a variety of mismatches in which some of the mismatches are located at the end of the strands (see fig. 13 and column 19, lines 47-50). Hogan et al. also disclose a set of nucleic acid probes which comprises three probes in which the 135 strand is interpreted as a third probe having a target hybridization region and an additional mismatch and a third probe is distinct from

another two probes (see fig. 7). In one system, arm region duplex formation comprises an active restriction enzyme cleavage site (see column 21, lines 10-12). A group of nucleic acid probes is disclosed in which at least two pairs of probes are involved (see fig. 6C, 6D, fig. 7). Each arm region of the probe has a unique sequence since the sequence of each arm region is not identical so that they form a unique combination (see fig. 7). A target is a nucleic acid sequence including essential sequences within the genome of a pathogenic organism, essential mRNA sequences produced by a pathogenic organism, and essential sequences within cancer cells (see column 4, lines 60-64).

Based on the analysis above, the teachings of Hogan et al. anticipate the limitations of the claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 34, 42-43, 57, 61-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. (5424413, issued, Jun. 13, 1995) as applied to claims 32-33, 35-41, 44-52, 54-56 and 58-60 above in view of Zhang et al. (5,876,924, issued March 2, 1999).

The teachings of Hogan et al. are set forth in section 5 above. Hogan et al. do not disclose that the T1 and T2 segments of the probe are capable of being ligated to each other when hybridized to S1 and S2 as recited in claim 34, a junction site between S1 and S2 as recited in

claim 57 and the method step (c) and (d) for detection of a target nucleic acid in a sample as recited in claims 61-63, and 67.

Zhang et al. disclose an improved method which allows for rapid, sensitive and standardized detection and quantitation of nucleic acids from pathogenic samples from a patient (see column 3, lines 11-15). The method applies a pair of non-overlapping oligonucleotide amplification probes (see column 3, lines 62-66). These probes are referred as a capture/amplification probe and an amplification probe (see column 3, lines 66-67) and are complementary to adjacent regions of a target (see column 4, lines 3-8) and do not overlap one another (see column 4, lines 8-9). The two probes join together by a ligating agent (see column 4, lines 9-11). The ligated amplification sequence is directly detected (see column 4, lines 16-19). The two amplification probes may be ligated to form contiguous sequence to be amplified (see column 4, lines 24-26). The polymerase chain reaction products are subject to electrophoresis for detection (see column 16, lines 25-35).

One of ordinary skill in the art would have been motivated to construct a probe comprising the terminal segments of the probe as taught by Zhang et al. which are able to be ligated when the terminal segments are hybridized to a target nucleic acid sequence at an adjacent position because the assembly of an amplifiable DNA by ligation increases specificity and makes possible a detection of a single mutation in a target (see column 3, lines 33-33). It would have been prima facie obvious to construct a terminal on each oligonucleotide probe which is able to be ligated when the terminal is hybridized to a target nucleic acid sequence at an adjacent position.

In addition, one of ordinary skill in the art would have also been motivated to apply an amplification method for detecting a target nucleic acid as taught by Zhang et al. because the method of Zhang et al. is an improved method which allows for rapid sensitive detection and can be performed in microtubes or a micro-well plate (see column 3, lines 19-27). It would have been prima facie obvious to perform the steps as recited in claims 61-69.

Hogan et al. do not disclose the limitations of claims 42-43 that the GC content in the arm region is higher than 80% or between 90% and 100%.

The capture/amplification probe designed for the method has a GC content at least 60%, and as such that they exhibit minimal secondary structure e.g. hairpin or fold back structure (see column 36, lines 1-3).

One of ordinary skill in the art would have been motivated to design an oligonucleotide probe comprising a GC content which is higher than 80% or between 90% and 100% as taught by Zhang et al. because by doing do so they exhibit minimal secondary structure e.g. hairpin or fold back structure (see column 36, lines 1-3). It would have been prima facie obvious to design an oligonucleotide probe which has a GC content which is higher than 80% or between 90% and 100%.

Hogan et al. do not disclose a kit comprising probes and reagents for detection of a target DNA sequence in a sample as recited in claims 70-72.

Zhang et al. disclose a kit which comprises probes and reagents for detection of an amplified ligated DNA sequences (see column 25, lines 7-36).

One of ordinary skill in the art would have been motivated to construct a kit including probes and reagents as taught by Zhang et al. because it was routine practice in the art for

conveniently performing a method. It would have been prima facie obvious to construct a kit as claimed.

Summary

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Joyce Tung/
Examiner, Art Unit 1637
August 3, 2009